REMARKS

I. Status of the Claims

Claims 1-35 were originally filed. As the result of a restriction requirement, claims 10-35 were withdrawn. Subsequently, claims 5 and 8-35 have been canceled. Claims 1-4, 6, and 7 are currently under examination.

II. Claims Rejections

A. 35 U.S.C. §101

The Examiner maintained the rejection of claims 1-4, 6, and 7 under 35 U.S.C. §101 for alleged lack of utility. Applicants respectfully traverse the rejection.

1. Standard to Assess Utility

According to MPEP §2107, the Examiner should review the claims and the supporting written description to determine whether the utility requirement under 35 U.S.C. §101 is met. No rejection based on lack of utility should be made if an invention has a well-established utility, *i.e.*, a utility that will be immediately appreciated by one of ordinary skill in the art based on the characteristics of the invention, regardless any such utility has been asserted. Neither should any rejection be made for lack of utility if an applicant has asserted a specific and substantial utility that would be considered credible by one of ordinary skill in the art.

According to *the Revised Interim Utility Guidelines Training Materials* ("the *Guidelines*") promulgated by the PTO (http://www.uspto.gov/web/menu/utility.pdf), a "specific utility" is a utility that is specific to the subject matter claimed, which contrasts with a general utility that would be applicable to the broad class of the invention.

The *Guidelines* further define a "substantial utility" as a "real world" use, which does not require or constitute carrying out further research to identity or reasonably confirm a "real world" context of use.

In most cases, an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101. MPEP §2107.02 III A. The Court of Customs and Patent Appeals stated in *In re Langer*:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of §101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

In re Langer, 183 USPQ 288, at 297 (CCPA, 1974, emphasis in original). To overcome the presumption of sufficient utility as asserted by an applicant, the Examiner must carry the initial burden to make a *prima facie* showing of lack of utility and provide a sufficient evidentiary basis for the conclusion. In other words, the Examiner "must do more than merely question operability--[he] must set forth factual reasons which would lead one skilled in the art to question objective truth of the statement of operability." *In re Gaubert*, 187 USPQ 664, 666 (CCPA 1975).

MPEP §2107.02 IV further states, a detailed explanation should be given for a utility rejection as to why the claimed invention has no specific and substantial asserted utility. Documentary evidence should be provided when possible. Otherwise the Examiner should specifically explain the scientific basis for his factual conclusions.

2. The Asserted Utility Is Specific and Substantial

The present specification provides, for the first time, the cloning of a Kir5.1 polypeptide. Pending claims are drawn to nucleic acids encoding Kir5.1 polypeptides, a class of inward rectifier K^+ channels. It is specifically asserted that the K^+ channels coded by the claimed nucleic acids "have significant roles in maintaining the resting potential and in controlling excitability of a cell" (*see, e.g.*, page 6, lines 24-25, of specification). Thus, the ion channels can be used as targets for treating disorders related to cell excitability, *e.g.*, hypertention, acute renal failure, chronic renal failure, diabetes insipidus, diabetic nephropathy, hypothyroidism,

hyperthyroidism, goiter, hypoparathyroidism, pancreatic insufficiency, diabetes, cystic fibrosis, sialorrhea, and salivary insufficiency, as described on page 6, lines 28-31, page 9, lines 19-24, and page 58, lines 15-21, of the specification.

The specification also states that the availability of gene sequences of these K^+ channels would enable assay systems to identify inhibitors or activators of the channels, which may be used for regulating physiological functions performed by the K^+ channels, such as modulating cell resting potential and in treating diseases related to cell excitability (*see, e.g.*, page 9, lines 11-27, of the specification).

Applicants assert that the present invention has a specific utility. Specific utility is defined by the MPEP and the *Guidelines* as a utility that is specific to the subject matter claimed. The MPEP further states that applications show sufficient specific utility when applicants disclose a "specific biological activity" and reasonably correlate that activity to a "disease condition." MPEP §§2107.01 and 2107.02.

In the present application, Applicants disclose a "disease condition," *e.g.*, any one of the diseases named above having altered cell resting potential and excitability, that correlates with a "specific biological activity," *i.e.*, the opening and closing of Kir5.1 inward rectifier K^+ channels, which lead to changes in cell resting potential and excitability. This application demonstrates the connections between Kir5.1 channel activity and cellular resting potential and excitability (*see, e.g.*, Example II on page 57, lines 19-28, of the specification). The application further provides methods for identifying compounds capable of modulating Kir5.1 channel activities, which may be used for treating diseases related to abnormal cell excitability, such as the diseases named above. Applicants thus submit that the present invention has established a specific utility, under the standards set forth by the MPEP, by demonstrating a reasonable correlation between a "specific biological activity"(*i.e.*, the Kir5.1 channels mediate cell resting potential and excitability) and a "disease condition" (*i.e.*, any of the above-named diseases related to abnormal cell excitability). Such a reasonable correlation is particularly clear in Kir5.1 channel activity and renal or thyroid diseases related to altered cell excitability (*e.g.*, acute renal

failure, chronic renal failure, hypothyroidism, hyperthyroidism, and hypoparathyroidism, among the above-named diseases) based on high level of Kir5.1 expression in the kidney and thyroid gland (*see* Table I on page 58 of the specification).

Applicants also assert that the present invention has a substantial utility or a "real-world" use. The present invention provides polynucleotide and polypeptide sequences of Kir5.1 inward rectifier K^+ channels, demonstrates that Kir5.1 channels modulate cellular resting potential and excitability, and teaches how to identify modulators of Kir5.1 channels. Therefore, there is a real-world use of the invention in the modulation of cell excitability, as well as in the identification of compounds that modulate Kir5.1 channels and thus can be useful as therapeutic agents for treating diseases related to altered cell excitability, such as any of the above-named diseases.

3. No *Prima Facie* Showing Has Been Made That the Asserted Utility Is Not Specific or Substantial or Credible

The Examiner's rejection of the pending claims for alleged lack of utility was based on the notion that the asserted utility of the present invention is not specific or substantial, although the Examiner conceded that the asserted utility is credible (*see, e.g.*, lines 2-4 of the first full paragraph on page 4 and lines 1-3 of the second full paragraph on page 5 of the final Office Action dated June 16, 2003).

Specifically, the Examiner has questioned the validity of the experiment illustrated in Figure 1 and Example II for lack of an absolute negative control and stated that such assays "can be performed with any polypeptide" (the first full paragraph on page 4 of the June 16, 2003, final Office Action). Applicants respectfully note that an absolute negative control, *i.e.*, cells expressing neither Kir5.1 nor Kir4.1, is not necessary for the experiment illustrated in Figure 1 and Example II to demonstrate the functions of the Kir5.1 polypeptide. Because the Kir5.1 functionality is shown through the comparison of current magnitude between the same host cells in which exogenous Kir5.1 alone or Kir5.1 plus Kir4.1 are introduced and expressed, the endogenous expression of Kir5.1 or Kir4.1 and any potential effects from such

expression are background and thus bear no relevance to the final results of the experiment. Applicants further note although the assay could theoretically be performed with any polypeptide, as the Examiner stated, polypeptides that are not ion channels are simply not expected to produce an effect similar to that observed in Figure 1 and Example II. In fact, there is no evidence at all that any inward rectifier K^+ channel other than Kir5.1 can produce the same effect. As such, Applicants submit that the experiment demonstrating Kir5.1 activity is scientifically valid and that the asserted utility based on Kir5.1 activity is specific.

The Examiner has further contended that the asserted utility of using Kir5.1 channel as a target for treating diseases caused by altered cell excitability is credible but neither specific nor substantial. As discussed in an earlier section, Applicants contend that such asserted utility is specific, as it is not generally applicable to any nucleic acid encoding any polypeptide; Applicants further contend that such asserted utility is substantial, as treatment of diseases or conditions related to abnormal cell excitability including those named above is a "real world" use. On the other hand, the Examiner has not pointed to anything that supports the notion that the asserted utility is not specific or substantial, as the terms are defined by the MPEP and the *Guidelines*. The Examiner instead stated, "[t]he specification discloses nothing about the normal levels of expression of the polynucleotide. The specification also does not disclose disorders or conditions associated with the Kir5.1 gene, either normal or mutated/deleted/translocated. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease or condition" (the sentence bridging pages 5 and 6 of the June 16, 2003, final Office Action).

Applicants believe that by making this statement the Examiner was in fact questioning the credibility of the asserted utility, and not whether the asserted utility is specific or substantial. As discussed in a previous section, raising a rejection for lack of utility based on the Examiner's disbelief of the asserted utility is inconsistent with the proper practice described in the MPEP, which places the initial burden on the Examiner, not Applicants, to provide evidence to support a factual conclusion of the credibility of an asserted utility. In fact, MPEP §2107.02 III.B. specifically cautions Office personnel that, once an assertion of a particular

utility is made, "that assertion cannot simply be dismissed ..... as 'wrong,' even when there may be reason to believe the assertion is not entirely accurate." Instead, the Examiner must provide an explanation setting forth the reasoning used in concluding that the asserted specific and substantial utility is not credible; support for factual findings relied upon in reaching the conclusion; and an evaluation of all relevant evidence of record, including utilities taught in the closest prior art. MPEP §2107.02 IV. The Examiner provided none of the above in challenging the credibility of the utility of the present invention as asserted by Applicants.

In summary, the Examiner's position that the asserted utility of the present invention is not specific or substantial is unsubstantiated. Neither has the Examiner carried the burden to show why the asserted utility is not credible. As such, no *prima facie* showing of lack of utility is made and the presumption of sufficient utility remains.

4. Claims Drawn to Nucleic Acids Encoding Fully Characterized Proteins Meet the Utility Requirement under 35 U.S.C. §101

The Kir5.1 channels are fully characterized both structurally and functionally. The nucleic acids encoding the Kir5.1 channels are defined by shared structural features, *e.g.*, they are capable of hybridizing to a reference sequence under specified conditions, and shared functional features, *e.g.*, they encode polypeptides capable of forming an inward rectifier potassium channel with at least one additional Kir alpha subunit.

According to the *Guidelines*, a characterized protein has sufficient utility for patentability. This standard is made evident from Example 8 of the guidelines. In Example 8, a compound A is disclosed to inhibit enzyme XYZ, a well known enzyme, *in vitro*. The specification states that the compound A can be used to treat diseases caused or exacerbated by enzyme XYZ. No such diseases are named. Claim 1 is directed to compound A. Claim 2 is directed to a method of treating a disease caused or exacerbated by enzyme XYZ consisting of administering an effective amount of compound A to a patient. In the subsequent analysis, claim 2 is deemed to be insufficiently supported by a real world context of use. This is because neither the specification nor the art of record discloses any disease or conditions caused or exacerbated

by enzyme XYZ and therefore, the asserted utility is seen as a method of treating an unspecified and undisclosed disease or condition, which does not define a "real world" context of use. Claim 1, however, is regarded as having utility because claim 1 is directed to a compound that inhibits an enzyme and enzymes have well established utility in the art, *i.e.*, catalyzing certain reactions.

This example can be compared to the present application. The present application claims nucleic acids encoding Kir5.1 potassium channels, which are analogous to compound A that inhibits enzyme XYZ. The specification states that Kir5.1 channels are likely involved in modulating cell excitability in various tissues. Thus, the ion channels can be used to as targets for treating disorders related to cell excitability. In Example 8, claim 1 directed to compound A is found to have utility even though there is no disclosure of specified disease that to be treated. Accordingly, even if the Examiner is not convinced, despite the disclosure by the present specification, that Kir5.1 channels are involved in regulation of cell excitability in certain tissues, a claim directed to compound A, *i.e.*, the nucleic acids encoding Kir5.1 potassium channels in the present case, have sufficient utility for patentability. The utility resides in the fact that the claimed nucleic acids encode inward rectifier potassium channels, which, like enzymes, have a well-established utility in the art: adjusting the passage of K^+ according to varying conditions.

Analysis of the pending claims according to the *Guidelines* therefore further supports Applicants' position that the rejection for lack of utility is improper.

In summary, Applicants do not believe that the rejection for lack of utility is properly substantiated and hence respectfully request its withdrawal.

B. 35 U.S.C. §112 First Paragraph

The Examiner also maintained the rejection of claims 1-4, 6, and 7 under 35 U.S.C. §112 first paragraph for alleged lack of enablement. The Examiner asserted that since no patentable utility has been established, one of skill in the art would not know how to use the claimed invention. As discussed above, the claimed invention does have utility under 35 U.S.C. §101. Accordingly, the enablement rejection on this basis should be properly withdrawn.

C. 35 U.S.C. §112 Second Paragraph

The Examiner also maintained the rejection of claims 1-4, 6, and 7 under 35 U.S.C. §112 second paragraph for alleged indefiniteness. Specifically, the Examiner stated that the stringent hybridization conditions in claim 1 do not sufficiently define the metes and bounds of the claimed subject matter, because the "comprising" language allows the presence of other ingredients in the hybridization or wash solution, which may lead to lower level of hybridization stringency and subsequently broader claim scope. The Examiner further suggested amending the claim language from "comprising" to "consisting of." Applicants respectfully disagree with the Examiner.

Claim 1 defines the stringency of hybridization based on the concentrations of SSC, SDS, and formamide in addition to temperatures of hybridization and wash. As one of ordinary skill in the art knows, there are many optional ingredients that can be included in the hybridization and wash solutions without altering the stringency of a hybridization. For example, to reduce nonspecific signals, a skilled artisan often includes in a hybridization solution carrier nucleic acids (*e.g.*, salmon sperm DNA), which have no effect on stringency. This is because the stringency of a hybridization is determined by the concentrations of monovalent cations (*e.g.*, Na^+ in SSC and SDS) and organic solvent (*e.g.*, formamide) as well as temperature, which are the components of the hybridization conditions specified in the claims. Applicants have attached a copy of pages 33-37 from Roche Applied Science product manual, as Exhibit A (http://www.roche-applied-science.com/prod_inf/manuals/InSitu/pdf/ISH_33-37.pdf), and a copy of pages 388-389 from Maniatis et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1982, as Exhibit B, to provide a general description of hybridization stringency and relevant factors.

Furthermore, Na^+ concentrations above 0.4 M in a hybridization solution are known to have only slight effect on hybridization stringency (second paragraph of the left column on page 33 of Exhibit A). In the present case, claim 1 recites a hybridization solution comprising 5 x SSC and 1% SDS. Since 5 x SSC contains 0.75 M NaCl and 0.075 M tri-sodium citrate, this hybridization solution has a Na^+ concentration clearly above 0.4 M. Therefore, even

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if any additional monovalent cations may be included in the hybridization solution as recited in claim 1, the level of stringency will not be significantly effected.

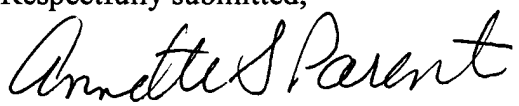
As such, Applicants submit that claim 1 as it is currently pending fully satisfies the requirement under 35 U.S.C. §112 second paragraph and that amending "comprising" to "consisting of" would unfairly and inappropriately limit the scope of claim 1 and its dependent claims. The withdrawal of rejection under 35 U.S.C. §112 second paragraph is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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